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The effect of gestational parity on FEV_1 in a group of healthy volunteer women

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In the past, studies utilizing within-subject comparisons of small groups of pregnant women showed that forced expiratory volume in 1 s (FEV_1) remained essentially unchanged during pregnancy. However, one of the findings from an epidemiological study was that women with greater number of children experienced a faster decline of FEV_1. The aim of this study was to examine the effect of parity on FEV_1 in a group of healthy volunteer women. To this end, cross-sectional multiple regression analyses of data from 397 healthy women participants in the Baltimore Longitudinal Study of Aging (BLSA) with a mean (range) age of 47·7 (18–92) years were performed. Similar analyses were done using the younger (50 years or less) and the older (>50 years) subgroups. After controlling for age, height, weight, and smoking, parity as a dichotomous variable was associated with a higher FEV_1 in women of child-bearing age (0·139 l; $P=0·02$) but not in the older women. There was a modest link with the number of children ($P=0·05$), with the first child possibly having the greatest effect on FEV_1. We could not account for the effect of parity on FEV_1 by the educational level, occupation, health status of the women, or by the presence of a cohort effect. Thus the nulliparous state is associated with lower FEV_1 in this group of healthy adult women of child-bearing age.

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Introduction

During pregnancy, the enlarging uterus progressively elevates the diaphragm, thereby decreasing the height of the thoracic cavity (1). This is compensated for by an increase in the anterioposterior and transverse diameters of the chest (1). Accompanying these anatomic alterations are hormonal changes in progesterone, oestrogen and prostaglandins, among others. Studies examining the effect of pregnancy on pulmonary function have shown that the tidal volume increases (2), the functional residual capacity and expiratory reserve volume decrease (3), but that forced expiratory volume in 1 s (FEV_1) is essentially unchanged (2–5). In these studies, changes in FEV_1 were determined by comparing FEV_1 in a few pregnant women with their FEV_1 after delivery. However, in a follow-up of the Cracow study (6), in which the risk of developing COPD was investigated, a faster FEV_1 decline was observed in women reporting a greater number of children. The authors suggested that this may be related to the poorer socioeconomic conditions in which these mothers live. No studies, however, have examined the effect of parity on lung function in normal women, or, if any such effect is found to exist, whether it is confined to the pre-menopausal period. This study was therefore undertaken to examine the effect of gestational parity on FEV_1 using healthy volunteer adult women.

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Methods

STUDY POPULATION

Subjects were female participants from The Baltimore Longitudinal Study of Aging (BLSA), a long-term, open-panel, multi-disciplinary study of normal human aging conducted by the National Institute on Aging which

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continuously enrolls self-recruited volunteers, primarily from the Washington–Baltimore area in the U.S.A. (7). The community-dwelling volunteer subjects, who are mostly white, well educated, and generally in good health at the time of entry into the study, undergo a battery of tests which include spirometry. They also completed the American Thoracic Society Division of Lung Diseases questionnaire (8). Of the 654 women who performed spirometric measurements between 1978 and 1994, we selected FEV_1 baseline values from 397 Caucasian women with reproducible spirograms, who were free of pulmonary disease (asthma, bronchitis, emphysema, shortness of breath, pulmonary congestion, bronchiectasis, interstitial lung disease or tuberculosis), and coronary heart disease (angina pectoris, history of myocardial infarction, Q-wave abnormality, or ST depression on exercise testing), and had complete smoking, and child-birth histories, and whose FEV_1 % predicted values were greater than 65. Due to the well documented effect of race on lung function, and because the small number of non-whites did not allow for valid subgroup comparisons, this analysis was limited to Caucasian females. The healthy participants, who ranged in age between 18 and 92 years (mean 47·7 years), provided information on their parity, pulmonary/smoking histories, educational and occupational background. The entire cohort was divided into younger (50 years or less) and older (>50 years) subgroups with mean ages of 34·2 and 65·9 years, respectively. The few twin births that were reported ($n=6$) were considered as a single parous experience. An overall score of the health status of the subjects (0=robust; 1=average; 2=limited; 3=ill) was given by the BLSA medical staff who performed the physical exams. Smoking classification is the same as reported previously (9,10). Current cigarette smokers are those who smoked cigarettes every day or who had stopped smoking less than 2 years before the date of visit. Never-smoking women are those who had not smoked more than 5–10 packs of cigarettes, 50–75 cigars, or three to five packages of pipe tobacco during their lifetime. In this study, the effect of smoking was evaluated by alternately comparing current smokers with subjects who are not currently smoking, and never smokers with ever smokers (10).

SPIROMETRIC METHODS

Spirometric measurements were performed as described earlier (9,10) using instruments that met the accuracy criteria of the American Thoracic Society. Spirometric results obtained prior to 1987 were converted to digital data to allow computerized assessment of quality and reproducibility, and only those participants with reproducible spirograms were included in this study. Reproducibility criteria were met when the second largest FEV_1 was within 5% of the largest value (9,10). FEV_1 % predicted was calculated by dividing the observed FEV_1 by the corresponding predicted FEV_1 values derived from the BLSA sex- and race-specific cross-sectional FEV_1 prediction equation (9), which for Caucasian women is:

$$FEV_1 = 0{\cdot}032 \times \text{height (cm)} - 0{\cdot}019 \times \text{age (years)} - 1{\cdot}52$$

STATISTICAL ANALYSES

Stepwise multiple regression models with FEV_1 as the dependent variable were used in cross-sectional analyses of the entire cohort and its two subgroups (SAS Software, SAS Institute, Cary, NC) (11). The independent variables were: age, height, weight, smoking status, parity, cohort group (defined in decades of date of birth) and years of education (surrogate for socioeconomic status). The latter was represented by a categorical variable (0=0–4; 1=5–8; 2=9–11; 3=12; 4=13–15; 5=16; 6=17 or more yr). Since the number of women with more than three or four children was low (2·5% in the entire cohort had more than 4 children, and 7% of the women in the younger subgroup had more than three children), parity was represented by a numerical variable ranging from 0 to 4 in the regression of the entire cohort and the older subgroup, and 0 to 3 for the younger subgroup. To check the validity of this representation, we repeated the analyses after excluding the few women whose parity exceeded 4 and 3 respectively. The coefficients of the predictors of FEV_1 were essentially unchanged.

We also represented parity by an ordinal categorical variable in an ANCOVA (analysis of covariance) of the entire cohort and the younger subgroup using PROC GLM in SAS (11). The categorical representation did not provide a significantly better fit than the numerical representation for either of the two groups ($P=0{\cdot}553$ and 0·423, respectively). Consequently, we represented parity by the numerical variable described above. In addition, since the number of nulliparous women, especially in the younger subgroup, was large (48·7%), we repeated the analysis using parity as a dichotomous variable (0=nulliparous, 1=one or more child).

To investigate further the role of socioeconomic factors on FEV_1, we obtained data on the current homemaking status and occupation of the women in the younger subgroup. The categorized codes for the variables current homemaking (0=not currently homemaker; 1=full-time homemaker; 2=part-time homemaker), and occupation (1=professional/technical; 2=manager; 3=clerical; 4=skilled craft; 5=semiskilled/labourer; 6=farmer; 7=student; 8=homemaker) were entered as categorical covariates in the full model of the younger subgroup using PROC GLM in SAS (11). To determine the effect of parity on FEV_1 % predicted in the younger sub-group, we repeated all of the above analyses with FEV_1 % predicted as the dependent variable. As before, the models were fitted using PROC GLM and Proc Reg in SAS (11) and the final model in the analysis was determined by backward elimination of the nonsignificant terms. Coefficients were considered significant at a P-value of 0·05.

Results

Table 1 shows baseline characteristics of the healthy BLSA women when grouped by age. Comparing those over 50 years of age with the younger subgroup shows that, on average, the latter had fewer children and a higher proportion of nulliparous women. While slightly over 50% of

TABLE 1. Baseline descriptive statistics for healthy BLSA women [mean (SD)]

	Age groups		
	Younger (18–50 years)	Older (51–92 years)	Younger+older (18–92 years)
Subjects (*n*)	228	169	397
Age (years)	34·2 (8·4)	65·9 (9·5)	47·7 (14·0)
FEV_1 (l)F	3·21 (0·45)	2·27 (0·51)	2·81 (0·67)
FEV_1 (% predicted)	100·3 (11·3)	100·1 (17·1)	100·2 (14·0)
Height (cm)	165·6 (5·9)	161·5 (6·2)	163·9 (6·3)
Weight (kg)	62·3 (10·6)	63·8 (10·5)	62·9 (10·6)
Number of children	1·1 (1·3)	2·2 (1·4)	1·6 (1·5)
Nulliparous (%)	48·7	16·6	35·0
Current smokers (%)*	17·5	13·0	15·6
Never smokers (%)*	55·3	50·3	53·1
Years of education (%)†			
9–11 yrs	0·9	3·0	1·8
12 yrs	7·4	11·2	9·1
13–15 yrs	20·2	21·9	20·9
16 yrs	35·5	25·4	31·2
17 or more yrs	36·0	38·5	37·0
Occupation (%)‡		—	—
Professional/technical	50·4	—	—
Clerical/sales	17·5	—	—
Semiskilled/labourer	3·5	—	—
Student	3·1	—	—
Currently homemaker (%)¶		—	—
Not homemaker	29·4	—	—
Full-time homemaker	24·1	—	—
Part-time homemaker	46·5	—	—

*Current smokers (0=no; 1=yes); *Never smokers (0=no; 1=yes).
Codes for years of education†, occupation‡ and current homemaker¶ are as in Methods (Statistical Analysis).

women in both subgroups were never smokers, the proportion of current smokers in the younger subgroup was somewhat higher than that in the older subgroup. The educational background of the subjects, as measured by years of education, indicated a high socioeconomic status. The lowest level of education in the overall sample was 9–11 years of schooling ($n=7$), with the majority (36% and 38·5% in the younger and older subgroups respectively) having completed 17 or more years of schooling.

Table 2 gives the coefficients of FEV_1 predictors from the final models, using the whole study group, the younger, and the older subgroups respectively, and with parity first as an ordinal variable then as a dichotomous variable. The estimates of the coefficient of age were almost identical and highly significant ($P<0·0001$) in all regressions regardless of the age group or the way parity was represented. The same was true for the estimates of the height coefficient. Current smoking was significant for the entire cohort and the older subgroup only, while never smoking was not significant in any of the regressions. When parity was represented by a numerical variable, it was significant in both the regressions of the entire cohort and the younger subgroup.

Representing parity by a dichotomous variable increased the estimates of its coefficients and their significance in the regressions of the entire cohort and the younger subgroup only, indicating that parity is associated with an increase of 0·139 l in the mean adjusted FEV_1 in the younger subgroup [Table 2(b)]. The fact that this increase was not observed in the older subgroup may be partly due to the substantially lower percentage of nulliparous women in this subgroup. To check this possibility, we calculated the power of detecting a statistical difference in the latter subgroup between the means of FEV_1 % predicted of the nulliparous women, and those with at least one child. In a simple two-sample comparison of means of FEV_1 % predicted of women in the older subgroup, the power of detecting a true difference of 2·1% (which is the actual observed difference between the means of FEV_1 % predicted of the nulliparous women and those who had one child or more) is only 8·5%. Hence the chance of committing a type II error is 91·5%. Similarly, the power of detecting a difference of 5·1% (the observed difference in the means of FEV_1 % predicted between the nulliparous younger women and those who are not) is only 26·3%.

TABLE 2. Coefficient estimates (*P*-value) of FEV_1 predictors from multiple linear regression models using different age groups of healthy BLSA women with parity as an ordinal variable (a) or dichotomous variable (b)

	(a) Entire cohort (18–92 years)	Younger women (18–50 years)	Older women (51–92 years)	(b) Entire cohort (18–92 years)	Younger women (18–50 years)	Older women (51–92 years)
Age (years)	− 0·0255 (0·0001)	− 0·0232 (0·0001)	− 0·0251 (0·0001)	− 0·0256 (0·0001)	− 0·0235 (0·0001)	− 0·0235 (0·0001)
Height (cm)	0·0347 (0·0001)	0·0355 (0·0001)	0·0326 (0·0001)	0·0345 (0·0001)	0·0353 (0·0001)	− 0·0326 (0·0001)
Current smoker (0=no; 1=yes)	− 0·1319 (0·0089)	n.s.	− 0·2748 (0·0013)	− 0·1347 (0·0076)	n.s.	− 0·2748 (0·0013)
Parity*	0·0285 (0·0513)	0·0528 (0·0449)	n.s.	0·0934 (0·0264)	0·1392 (0·0171)	n.s.
Weight (kg)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Cohort group†	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Education‡	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Occupation‡	—	n.s.	—	—	n.s.	—
Currently homemaker‡	—	n.s.	—	—	n.s.	—
R^2	0·70	0·38	0·47	0·71	0·39	0·47

*Parity represented in (a) as : 0,1,2,3,4+ for the entire cohort and the older subgroup, and as: 0,1,2,3+ for the younger subgroup. In (b) parity was represented as dichotomous variable for all groups (0=nulliparous; 1=1 or more child). SEMs of the coefficients of parity for the entire cohort and the younger women (a) were 0·0146 and 0·0262 respectively. In (b) the respective values were 0·0419 and 0·0580.
†Cohort groups defined in decades of date of birth.
‡Codes for education, occupation and current homemaker are as in Methods.
n.s., Not significant ($P>0·1$).

Table 2 also shows that weight, as well as the coded variables for cohort group and years of education, when included in the analyses as described earlier, were not statistically significant in any of the models. To check the possibility that colinearity between age, parity, and smoking could have influenced the results, we calculated the variance inflation factors (VIF) for these variables in the regressions (12). The results indicated that colinearity between these variables was not a serious concern in these regressions.

Having shown that parity is associated with a higher FEV_1 in the younger subgroup, it was important to consider other relevant socioeconomic variables which may account for the observed increase. Consequently, we retrieved information on the occupation and current homemaking status of the younger women. Table 1 shows that the majority of women in this subgroup (50·4%) were in a professional or technical field (doctor, lawyer, engineer, accountant, teacher, nurse) while 17·5% had clerical (secretarial, book-keeping) or sales (insurance agent, sales clerk, salesman, real estate agent) jobs, and 3·5% were classified as semiskilled/labourer (waitress, cashier). This result is consistent with the high level of education and socioeconomic status of the BLSA participants. Table 1 also shows that in the younger subgroup, the majority (47%) were part-time homemakers, probably career women who are also homemakers, while 29% of the women were not currently homemakers. It is interesting to note that 76% of the women in the latter group were under the age of 30 (91% <40 years of age), and 96% were nulliparous. Table 2 shows that the coded variables for occupation and current homemaking status when included in the full model were not significant regardless of the way parity was represented.

The general health status of the participants (as described in Methods) is another possible confounding variable which could account for the observed increase in FEV_1. However, due to missing data, information was available on 384 women of the entire cohort and 220 of the younger subgroup (97% of each data set). In both groups, 29% of the subjects enjoyed robust health, and 70% were of average health. Analyses of the two incomplete data sets for the purpose of assessing the effects of the subjects' health on FEV_1 and FEV_1 % predicted indicated that the overall health score was not a significant predictor of FEV_1 or FEV_1 % predicted in this study group (results not shown).

When the effect of having children on FVC was also assessed by regression analysis with age, height, weight, parity and smoking as independent variables, parity was found to be significant in the entire cohort and the younger subgroup, but not in the older subgroup. In the former two groups, the coefficients for parity as a dichotomous variable were 0·144 ($P=0·004$) and 0·164 ($P=0·021$), respectively. Consequently, for women in the younger subgroup, parity was associated with a larger FVC. The magnitude of the effect on the mean adjusted FVC was 0·164 l.

To examine the possibility that the effect of parity in the younger subgroup may be due to the inclusion of the predominately nulliparous women who are younger than 25 years ($n=42$), and whose lungs may not have reached full development, we repeated the analysis using women between 25 and 50 years. When parity was represented by a dichotomous variable in the above analyses, where the

TABLE 3. Effect of parity on mean FEV_1 % predicted (SD) in the younger subgroup (18–50 years) of healthy BLSA women when parity was represented by a continuous variable (a) or by a dichotomous variable (b)

(a) Parity	*n*	Mean FEV_1 % predicted* (SD)	(b) Parity	*n*	Mean FEV_1 % predicted** (SD)
0	111	97·7 (10·5)	0	111	97·7 (10·5)
1	35	102·4 (11·6)	1 or more	117	102·8 (11·5)
2	45	102·9 (10·7)			
3 or more	37	103·1 (12·4)			

*$P=0·0078$; **$P=0·0006$; $n=228$.

dependent variables were FEV_1 and FVC, the coefficients for parity were 0·146 ($P=0·0150$) and 0·189 ($P=0·0091$) respectively. These coefficients were larger in magnitude and statistical significance than those obtained when women younger than 25 years of age were included in the analysis (compare with 0·139 and $P=0·0171$ in the analysis of FEV_1 [Table 2(b)], and 0·164 and $P=0·021$ in the analysis of FVC (see above).

FEV_1 % predicted was also substituted for FEV_1 as the dependent variable in the analyses of the younger subgroup. Of all the variables listed in Table 2, only parity was found to be significant (Table 3). The incremental increase in FEV_1 % predicted appeared to be largest after the birth of the first child [Table 3(a)].

Discussion

The results from this study suggest that parity in this group of healthy, well-educated volunteer women is associated with a larger FEV_1. The effect is greater when parity is represented by a dichotomous rather than an ordinal variable. Similar associations of FVC with parity were observed. The larger values of FEV_1 and FVC with parity are attributed to women in the child-bearing age since they were not observed in the older subgroup. However, the failure to detect a statistically significant effect, for example, on FEV_1 % predicted in the older subgroup may, in part, be due to the lower statistical power resulting from the lower percentage of nulliparous women in this subgroup, thereby resulting in a Type II statistical error as shown earlier.

The difference in lung function between nulliparous and parous younger women persisted when the comparison was limited to the women who are 25–50 years old. This indicates that the observed effect cannot be attributed to the 18–25-year-old women of this study, who are overwhelmingly nulliparous, and whose lungs may not have reached full development.

The effect of weight (13), socioeconomic status and smoking history in the younger subgroup could not be invoked to explain this finding since parity was associated with increased body weight and body mass index (14). Moreover, the proportion of women with the highest levels of education and occupation decreased as parity increased. Similarly, the proportion of never smokers decreased, and that of current or former smokers increased as parity increased. More importantly, multiple linear regression analysis showed that the apparent effect of parity on FEV_1 in premenopausal women cannot be accounted for by the smoking history, weight, cohort effect, level of education, occupation, current homemaking status, or the general health of the subjects. Contrary to our findings in the younger subgroup, current smoking was found to be a negative predictor of FEV_1 in the older subgroup, even though the proportion of current smokers was slightly lower than that in the younger subgroup. This may be due to the difference in the length of the smoking period between the two groups, to the fact that the negative effects of smoking are not apparent during the early decades of life, or to selection bias.

The short-term effects of pregnancy on pulmonary function have been examined in depth in the past. According to Cameron *et al.* (15), hormonal changes may be responsible for the increase in thoracic width which takes place during pregnancy. Progesterone, which increases dramatically by late pregnancy, exhibits smooth muscle and ligament relaxing effects (16). In addition, hydrocortisone concentration in late pregnancy was shown by Cope and Black (17) to increase more than two-fold as compared with the nonpregnant levels. The total pulmonary resistance was reported to be reduced in late pregnancy, possibly due to alterations in the smooth muscles of the tracheobronchial tree induced by relaxin or corticosteroid (18). It is interesting to speculate that the hormonal changes during pregnancy which were postulated to cause the observed increase in thoracic width (15) and the decrease in pulmonary resistance (18) may be responsible for the small observed increases in FEV_1 and FVC that persist during the child-bearing years. Among other known beneficial associations with pregnancy is the decline in blood pressure which mirrors the hormonally modulated drop in vascular resistance (19).

Our results are contrary to that of the Cracow follow-up study (6). One plausible explanation is that offered by the authors who suggested that the larger decline in FEV_1 observed in mothers with high parity may be due to their worse socioeconomic conditions (6). Our study group had a relatively homogeneous and high socioeconomic status. The only other instance where parity was associated with enhanced pulmonary function was reported by Horne *et al.* (20) who showed that in women with moderate protease

inhibitor (Pi) deficiency, pulmonary function was significantly better with increasing number of children, possibly due to the pregnancy-induced increase in Pi levels.

The subjects in this study were self-recruited volunteers who were generally well educated and financially comfortable, as shown by the high number of professional and career women. After undergoing a battery of tests and answering a variety of health and background questionnaires, we selected a group of healthy and well-characterized women who, as it turned out, had a high proportion of nulliparous women. Consequently the study group was not representative of the general population. On the other hand, it may well be that in order to assess the effect of having children on lung function, we need a group such as this where health and socioeconomic factors are not limiting and therefore cannot mask the effect of parity on FEV_1 and FVC.

The parity-associated gain in FVC is consistent with the hypothesis that the pregnancy-induced increase in thoracic width is responsible for the rise in FEV_1. The magnitude of the effect of nulliparity on pulmonary function is estimated using the coefficients of parity in the regressions of FEV_1 [Table 2(b)] and FVC (see above). Therefore, the mean adjusted decreases in FEV_1 and FVC that, for example, a 30-year-old nulliparous woman is expected to have relative to another with one or more child are 0·139 l and 0·164 l, respectively.

It is important to mention that, in contrast to the FEV_1 values which were subjected to a quality assurance program that met current ATS standards, some of the earlier FVC values were not obtained in a manner consistent with the current ATS recommendations which require a complete plateau. However, since the less than ideal FVC results include women of all parity groups, we decided to present the FVC results in support of our finding that parity was associated with a relatively higher FEV_1.

The use of years of education as a surrogate for socioeconomic status is appropriate since the former variable is a stable measure of social and economic conditions that affect health. The occupational and current homemaking status are less accurate measures of socioeconomic status, especially in women. Career interruptions due to childbearing and homemaking, as well as the hiring of domestic help, lead to errors and discrepancies in the reporting of occupation and home making status.

The clinical significance of our findings is unknown, and will require confirmation in other groups of women. However, the size of the observed effect is large in comparison to other predictors of lung function. Women in the younger subgroup, aged 18–50 years, had a mean adjusted FEV_1 which was 0·139 l larger if they had borne children. This is similar in magnitude, although opposite in direction, to the effect of tobacco smoking on FEV_1, and would be comparable to 4–5 years of decline in lung function. While the results of our study may be due to the selection of women with better lung function to bear children, it should be emphasized that all of our participants underwent extensive testing to detect clinical abnormalities. The magnitude of the effect of parity on lung function observed in the present study, if confirmed by others, would make this an important predictor of lung function. Thus epidemiological and clinical studies of lung function in younger women would need to include information about gestational parity.

In summary, this cross-sectional study of healthy, well-educated volunteer women shows that parity is associated with a somewhat larger FEV_1 during the child-bearing age. A similar increase was observed in FVC. Further investigation is needed to find out whether the observed parity-associated increase in pulmonary function can be confirmed in other groups of women, and if it persists in older women. Thus the nulliparous state is associated with lower lung function.

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